CDC
CENTERS FOR DISEASE CONTROL AND PREVENTION

FACTS

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The CDC-sponsored External Consultants Meeting on Antiretroviral Therapy for Potential Nonoccupational Exposures to HIV July 24-25, 1997 Atlanta, Georgia

The most effective methods for HIV prevention remain those that prevent exposure to HIV in the first place. Attempting to prevent HIV infection by taking antiretroviral therapy should never take the place of adopting and maintaining behaviors that prevent HIV exposure. These include sexual abstinence, having sex only with an uninfected partner, consistent and correct condom use, abstinence from injection drug use, and consistent use of clean equipment for those who are unable to cease injection drug use. In recent years, the Public Health Service (PHS) has recommended the use of antiretroviral drugs to reduce (1) HIV acquisition among those exposed in the workplace (e.g., accidental needle-sticks received by health care workers) and (2) perinatal HIV transmission. Questions have arisen about whether antiretroviral drugs should be offered to people with unanticipated sexual or drug injection-related exposures to HIV. However, no data currently exist about the effectiveness of such therapy for these types of exposures.

On July 24 and 25, 1997, the Centers for Disease Control and Prevention (CDC) and its prevention partners invited experts to share their insights, knowledge, and uncertainties about providing antiretroviral therapy to people with nonoccupational exposures to HIV. This document provides a short summary of that meeting.

What is meant by antiretroviral therapy for exposures to HIV?

This refers to using antiretroviral drugs in an effort to reduce the chances of HIV infection after a person has been exposed to the virus. Clinicians also refer to this preventive therapy as post-exposure prophylaxis (PEP).

What is meant by "nonoccupational exposure"?

This refers to any exposure to HIV that occurs outside the performance of a health care-related job or occupation. It typically refers to exposure through unprotected sex or sharing needles with HIV-infected persons, or to infants' exposure from infected breast milk. While occupational exposures are primarily accidental, one-time events, nonoccupational exposures may occur repeatedly.

What issues were discussed at the July meeting to consider the use of antiretroviral drugs for potential exposures to HIV?

Experts attending the meeting were asked to (1) consider the implications of existing research on the use of antiretroviral drugs for nonoccupational HIV exposures; (2) discuss the safety and efficacy of antiretroviral drugs for such use; (3) discuss factors related to the possible use of antiretroviral drugs for HIV exposures

if recommended; and (4) suggest mechanisms for reinforcing behavioral risk-reduction efforts while providing antiretroviral drugs.

(1) Existing research and its implications on the use of antiretroviral drugs for nonoccupational HIV exposures

In 1994, using surveillance data from health care workers in France, the United Kingdom, Italy, and the United States, a case-control study documented that although failures occurred, the use of zidovudine (ZDV) for postexposure prophylaxis was associated with an approximately 81% decrease in the risk for HIV infection after percutaneous exposure to HIV-infected blood (Cardo 1997). During the meeting, the investigators pointed out the study's limitations, including the facts that cases and controls were not matched and came from two separate populations; cases were often reported anecdotally; and details of the exposures were obtained retrospectively, whereas the information on controls was gathered prospectively. These and other factors may have introduced bias, possibly overestimating the magnitude of the protective effect. In addition, the validity of extrapolating those results to nonoccupational exposures was questioned.

In a clinical trial of ZDV administered to HIV-infected women during pregnancy and labor and to their infants for 6 weeks after birth, there was a 67% reduction in perinatal transmission. Since the reduction in maternal viral load did not correlate completely with protective efficacy, researchers hypothesized that other factors, including postnatal therapy for the infant, must have contributed to protection (Sperling 1996).

Experts also considered the importance of early events in HIV infection and replication. These discussions suggested there is a period following exposure to HIV and prior to established infection during which HIV may be vulnerable to suppression with antiretroviral drugs so that infection does not occur.

There are no human studies of antiretroviral drug therapy for sexual, drug use, or other non-occupational exposures to HIV. A variety of animal studies suggest potential benefits of the use of antiretroviral therapy after exposure to HIV. However, limitations of the animal data include lack of information regarding mucosal exposures, differences in drugs used, differences in drug metabolism between humans and animals, and the use of simian virus, which differs from HIV, in some experiments.

(2) The safety and efficacy of antiretroviral drugs used for potential nonoccupational exposures to HIV

Potential benefits have to be weighed against the significant health risks and costs associated with this therapy for nonoccupational exposures. First, these medications can have severe side effects (e.g., liver inflammation, kidney stones). Second, efficacy is unknown but is likely to be imperfect. If a person becomes infected despite taking antiretroviral medication, there is a theoretical risk that the viral strain will become resistant to the medications. And third, a 4-week course of these medications will cost $600-$1,000, which in many cases will not be covered by insurance.

This therapy should never be routine. It is a complicated medical therapy that should never be considered a desirable form of primary HIV prevention. This therapy is NOT a "morning-after pill."

(3) Factors related to the possible use of antiretroviral drugs for potential nonoccupational exposures to HIV

Many issues were discussed concerning the possible appropriate use of such therapy, including the following:

- the likelihood that the source is infected with HIV
- the likelihood of transmission, including the many cofactors that might increase or decrease transmission risk
- characteristics (e.g., viral load, stage of infection) of an HIV-positive source
- isolated versus recurrent HIV exposures
- time delay between possible exposure and presentation for medical care
- ability to adhere to the antiretroviral regimen

(4) Mechanisms for reinforcing behavioral risk-reduction efforts

There is broad-based concern that people may initiate or resume risky behaviors because of the perception that using antiretroviral drugs for HIV exposures is a "cure" for HIV infection. Widespread use of antiretroviral drugs for HIV exposures, if accompanied by increased levels of risky behavior, may increase the number of new HIV infections if more people are exposed to HIV because of a misguided reliance on antiretroviral drugs as their primary protection strategy. On the other hand, many studies have shown that behavioral interventions are effective in preventing HIV exposure and infection.

Are there existing recommendations for use of antiretroviral drugs after exposures to HIV?

Yes. Antiretroviral drugs currently are recommended for occupational exposure to HIV. In June 1996, CDC issued "Update: Provisional Public Health Service (PHS) Recommendations for Chemoprophylaxis after Occupational Exposure to HIV." These recommendations update the 1990 "PHS Statement on Management of Occupational Exposure to HIV, including Considerations Regarding Zidovudine Postexposure Use."

As a part of the "USPHS Task Force Recommendations for Use of Antiretroviral Drugs During Pregnancy for Maternal Health and Reduction of Perinatal Transmission of Human Immunodeficiency Virus Type 1 in the United States," zidovudine is recommended for women during pregnancy, labor, and delivery, and for infants for a few weeks after exposure to HIV at birth. However, it is not known whether treating infants *alone* will reduce the risk of infection in infants born to HIV-infected mothers.

There are no existing recommendations for the use of antiretroviral drugs after nonoccupational exposure to HIV.

What was the final outcome of the meeting?

In addition to the above issues, consultants considered what factors in specific scenarios would most influence their decision to use antiretroviral drugs for potential nonoccupational exposures to HIV. Speakers reviewed available information on how often and to whom potential exposures occur, the potential risks of using antiretroviral drugs after nonoccupational HIV exposures, and rates of adherence to and side

effects from these medications following occupational exposures. Cost-benefit analysis of the use of antiretroviral drugs following nonoccupational exposures to HIV and implementation, ethics, and public policy issues were discussed.

CDC affirms that efficacy data and additional epidemiological information are needed (e.g., the number of infections that could be averted by antiretroviral drugs, the number of people who would need to be treated to avert one infection, effects of antiretroviral drug availability on risk behavior, physician practices in prescribing antiretroviral drugs) before public policy recommendations can be formulated. Many more questions have been raised and many experts at the meeting urged that caution should be used in future decision making until more data are available. A PHS Working Group will deliberate on the proceedings and develop a statement for public comment later in 1998. Currently, the use of antiretroviral drugs for nonoccupational exposures to HIV should be considered a clinical intervention of unproven efficacy. Individual practitioners and their patients may opt to consider its use in specific circumstances following exposures to HIV that carry a particularly high risk of infection, but only after careful consideration of the potential risks and benefits and with a full awareness of the many gaps in our current knowledge.

Note:

CDC realizes that some physicians may wish to prescribe antiretroviral drugs for nonoccupational exposures to HIV. If local expertise is unavailable, physicians may wish to contact one of the following PHS staff for more information regarding antiretroviral drug issues in specific circumstances:

Adults	Dawn Smith, M.D.	404-639-6146 (e-mail: dks0@cdc.gov)
Children	Kenneth Dominguez, M.D	404-639-6133 (e-mail: kld0@cdc.gov)
Pregnant women	Lynn Mofensen, M.D.	301-496-7339 (e-mail: lm65d@nih.gov)

National Center for HIV, STD & TB PREVENTION

For more information...

CDC National AIDS Clearinghouse:

P.O. Box 6003
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CDC National AIDS Hotline:

1-800-342-AIDS
Spanish: 1-800-344-SIDA
Deaf: 1-800-243-7889

CDC National STD Hotline:

1-800-227-8922

CDC DHAP Internet home page address:

http://www.cdc.gov/nchstp/hiv_aids/dhap.htm

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***A free copy is available by contacting the CDC National AIDS Clearinghouse**